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(19)

(54) IMPROVEMENTS IN OR RELATING TO SOLUBILIZED ALGINIC MATERIALS

(71) We, WALLACE, CAMERON AND COMPANY LIMITED, a British Company of Ultra House, Drakemire Drive, Castlemilk Industrial Estate, Glasgow, S.5, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to a new method of manufacturing metal/alginic acid salts.

It is known that solubilized alginic materials such as sodium alginate and sodium calcium alginate have high utility as haemostatic agents and accordingly they are widely used in surgical and medical dressings and bandages; alginates are used also in the textile field.

It has been proposed previously to treat water-insoluble calcium alginate with a salt of ethylene diamine tetracetic acid, the said salt containing a solubilizing cation. The solubilizing cation exchanges with the calcium to impart solubility to the alginate. The magnesium salt of ethylene diamine tetracetic acid may be used, in which case the product is calcium magnesium alginate which is more soluble than calcium alginate itself. When this process is applied to calcium alginate in the form of a gauze, the exchange of ions takes place on the surface of the gauze to coat same with the soluble alginate.

It has been proposed also to treat alginic acid with a compound of a metal to form, by neutralisation, the alginate of the said metal.

According to the present invention, there is provided a method of preparing a solubilized alginic material comprising reacting a soluble aginate of sodium, potassium or ammonia with an ionic compound of copper, silver, mercury, cadmium, magnesium, zinc, iron, boron or aluminium, to replace some of the sodium, potassium or ammonium ions.

The soluble alginate is preferably soluble calcium sodium alginate, and the ionic compound is preferably a compound of zinc, silver or aluminium. In a preferred form of the invention, the soluble aginate comprises sodium calcium alginate, and the compound is a silver compound.

The alginate may be sodium alginate and the ionic compound may be zinc sulphate, aluminium hydroxide or silver nitrate. The reaction is preferably effected in a mixture of an alcohol and water and more preferably in a mixture of Industrial Methylated Spirit (I.M.S.) and water, preferably in a volume ratio of 80:20. Isopropyl alcohol may be used in place of I.M.S.

The following examples are given to illustrate the present invention in more detail:

EXAMPLE 1

A roll of calcium alginate gauze weighing 9 lbs 10 oz, and having a moisture content of 17.56% w/w, and a calcium content of 7.94% w/w based on the dried material was converted substantially completely to sodium alginate by the method of our Patent No. 1,231,506. The sodium alginate obtained analysed as follows:—

Moisture content — 15. 87% w/w
Calcium content — 0.1493% w/w
Sodium content — 11. 45% w/w

It is known that a calcium/sodium alginate containing from 3% to 5% w/w calcium has the most desirable solubility consistent with a high haemostatic property, and this is equivalent to 4.82 to 8.16% w/w zinc. Accordingly, a quantity (approx. 770 gm) of zinc suphate [$Zn\,SO_4 . 7H_2O$], in excess of the calculated amount necessary to provide 4.82% w/w zinc in the end product, was dissolved in 15 gallons of an 80:20 v/v mixture of I.M.S. and water, and the sodium

alginate gauze was circulated through this solution for 30 minutes. The material was then wrung and air dried. In a series of five runs, starting from similar calcium alginate gauzes, the following results were obtained:—

TABLE I

Run	Moisture Content % w/w	Na Content % w/w	Ca Content % w/w	Zn Content % w/w
1	18.09	7.20	0.156	7.24
2	18.57	6.64	—	7.20
3	18.38	7.31	0.205	6.68
4	18.16	7.32	0.208	6.88
5	18.26	7.90	0.202	6.84

The sodium and calcium contents were found by flame photometry and the zinc content was determined by complexometric titration with Eriochrome Black T as indicator and ammonia buffer.

The zinc content was rather higher than expected, but it is evident that zinc has replaced sodium, with the elimination of sodium sulphate, in all the runs. Each of the five products is soluble and is considered to have excellent healing properties in the treatment of varicose ulcers when applied thereto in the form of a gauze bandage or pad, by release of minute quantities of zinc in infected areas. It is known that zinc sulphate tablets taken orally in a dose of 220 mg thrice daily by patients suffering from varicose ulcers lead to alleviation of the ailment much more quickly than other forms of medication. Also, patients deficient in zinc heal more slowly than patients with adequate amounts of zinc, and it is considered that acceleration of blood clotting and of healing mechanisms can be obtained by application of sodium zinc alginate to wounds.

EXAMPLE 2

A) To an approximately 1% w/v solution of sodium alginate in water was added a saturated solution of zinc sulphate which resulted in the formation of a voluminous opaque slimy precipitate which clumped together in masses. The precipitate was stirred continuously for 30 minutes, the masses breaking down to give a material having a fibrous feel and which was filtered, pressed and dried to give a paper-like product which is considered to be suitable for the manufacture of wadding or pads for use in haemostasis.

B) Zinc sulphate solution was added in a continuous stream from a burette with a fine orifice, to a 1% w/v solution of sodium alginate in water to produce a fibre which on drying appears to have sufficient strength to enable it to be woven or knitted and further processed to produce a sodium zinc alginate gauze, in a manner similar to that in which calcium alginate gauze is produced.

EXAMPLE 3

A sodium aluminium alginate gauze was prepared in a manner similar to that described in Example 1, by taking 10 lbs of calcium alginate gauze with a moisture content of 17.16% w/w and a calcium content of 7.87% w/w, and acidifying the same by stirring it with 1,305 ml of conc. hydrochloric acid in 15 gallons of water, followed by conversion to sodium alginate by means of alcoholic sodium hydroxide.

A 3% w/w calcium gauze is suitably soluble and this is equivalent to 2.025% w/w aluminium. The amount of aluminium necessary to give a sodium aluminium gauze containing 2.025% w/w aluminium is 76.10 g, and this is equivalent to 305.9 g of dried Aluminium Hydroxide Gel B.P. which contains 47% by weight Al_2O_3. Accordingly, 305.9 g of this grade of $Al(OH)_3$ was dissolved in just sufficient dilute hydrochloric acid and this was then diluted with 15 gallons of I.M.S./water in a volume ratio of 80:20, the sodium alginate gauze was constantly circulated through this solution for 30 minutes and was then wrung and air-dried. From a series of runs, the following results were obtained:—

TABLE II

Run	Moisture Content % w/w	Na Content % w/w	Ca Content % w/w	Al Content % w/w
1	23.25	10.44	0.92	1.69
2	23.09	10.13	1.14	1.77
3	23.95	10.08	0.89	2.13
4	23.48	9.68	0.96	2.28

Aluminium has a protein precipitation action which gives an increased haemostatic action and possibly a bactericidal action, and hence the sodium aluminium alginate gauzes produced as above may find application in the field of haemostatic dressings, as for the known haemostatic alginates and sodium zinc alginate.

EXAMPLE 4

A silver calcium sodium alginate was produced by manufacturing calcium sodium alginate in accordance with the method of our Patent No. 1,231,506, and reacting this with a soluble silver salt. The calcium sodium alginate was very carefully washed free of sodium hydroxide to prevent precipitation of silver hydroxide. 15 gallons of silver nitrate solution in 80:20 v/v I.M.S./water was prepared from sufficient silver nitrate to produce a gauze containing 1%

w/w silver, which was a dark grey in colour, the calcium sodium alginate being treated in the silver nitrate solution analogously with the treatment in Examples 1 and 3.

It is considered that the silver calcium sodium alginate gauze will prove its efficacy as a burn dressing since silver ion has a specific bactericidal action against *Pseudomonas*, which bacteria are detrimental to the healing of burns. In addition, there is the usual haemostatic property.

The above Examples are given as illustrative only, and it is envisaged that alginates containing, besides sodium, potassium or ammonium, say iron, may be produced, for example in the form of an ammonium calcium iron alginate, iron being useful in the treatment of anaemia. Also, the alginate may be in the form of a powder for use in, for example, haemostatic aerosol preparations, in which case, the method of preparation will be similar to that described above although perhaps supplemented by filtration steps.

By virtue of the present invention alginic materials containing elements useful in therapeutic treatment of patients suffering from various ailments may be prepared, and these are considered to be useful in a wide range of applications.

WHAT WE CLAIM IS:—

1. A method of preparing a solubilized alginic material comprising reacting a soluble alginate of sodium, potassium or ammonia with an ionic compound of copper, silver, mercury, cadmium, magnesium, zinc, iron, boron or aluminium, to replace some of the sodium, potassium or ammonium ions.

2. A method of manufacturing a solubilized alginic material as claimed in claim 1, wherein the alginate is calcium sodium alginate and the ionic compound is a compound of silver, aluminium or zinc.

3. A method of manufacturing a solubilized alginic material as claimed in claim 1, wherein the alginate is sodium alginate and the ionic compound is zinc sulphate, aluminium hydroxide or silver nitrate.

4. A method of manufacturing a solubilized alginic material as claimed in any one of claims 1 to 3, wherein the reaction is effected in a mixture of an alcohol and water.

5. A method of manufacturing a solubilized alginic material as claimed in claim 4, wherein the alcohol is Industrial Methylated Spirit.

6. A method of manufacturing a solubilized alginic material as claimed in claim 4, whrein the alcohol is isopropyl alcohol.

7. A method of manufacturing a solubilized alginic material as claimed in claim 4 or claim 5, or claim 6 wherein the alcohol/water mixture is in a volume ratio of 80:20.

8. A method of manufacturing a solubilized alginic material as claimed in any one of claims 1 to 7, wherein the alginate is in the form of a gauze.

9. A method, according to claim 1, of manufacturing a solubilized alginic material, substantially as hereinbefore described.

10. A method of manufacturing a solubilized alginic material according to any one of the Examples.

11. A solubilized alginic material whenever manufactured by the method of any one of claims 1 to 10.

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